above amendments and the following remarks, Applicants respectfully request reconsideration of this application and allowance of the claims, as amended.

Claims 9-12 were objected to as being a substantial duplicate of claims 5-8. This has been corrected by amendment above. In view thereof, withdrawal of the objection is respectfully requested.

Claims 1-15 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite. By amendment above, claim 1 has been rewritten as two separate independent claims as suggested in the Office Action, and each indicated occurrence of indefiniteness has been corrected. Accordingly, withdrawal of the indefiniteness rejection is respectfully requested.

Claims 1-4 and 13-15 were rejected under 35 U.S.C. §102(e) as being anticipated by Sodemann U.S. Patent No. 6,166,007. This rejection is respectfully traversed.

The Sodemann patent issued December 26, 2000 on an application filed May 10, 1999, claiming the benefit of Provisional Application No. 60/091,491, filed July 2, 1998.

35 U.S.C. §102(e) is applicable where an invention in an application is described in a patent granted on an application by another filed in the United States before the invention thereof by the Applicant for patent.

In the present case, the invention is a method involving "forming a seal" (amended claim 1) or first contacting a surface with an anticoagulant agent and thereafter contacting the surface with a taurolidine and/or taurultam solution (new claim 24).

However, Sodemann Provisional Application No. 60/091,491 fails to provide any disclosure whatsoever of "forming a seal" as required by claim 1, or the first and second contacting as required by new claim 24. A copy of Sodemann Provisional Application No. 60/091,491 is provided herewith as Exhibit A.

The "administering to the device" set forth in the abstract and claim 1 of Sodemann U.S. Patent No. 6,166,007, referred to at page 3, last paragraph of the Office Action does not meet the above limitations set forth in present claims 1 and 24.

Example 2 of Sodemann U.S. Patent No. 6,166,007, referred to in the Office Action at page 3, last paragraph thereof, is not present in Provisional Application No. 60/091,491, but was added on May 10, 1999 when Serial No. 09/307,916 was filed.

Since Sodemann Provisional Application No. 60/091,491 provides no disclosure of the above-noted features of claim 1 and 24, for purposes of 35 U.S.C. §102(e) the

"invention" described in Sodemann U.S. Patent No. 6,166,007 has an effective filing date of May 10, 1999, which is after the March 29, 1999 provisional filing date of the present application. The present Applicant's Provisional Serial No. 60/126,940, filed March 29, 1999, clearly discloses at page 4, lines 25 and 26, that "solutions may conveniently be used to fill, flush or seal the delivery system when not in use." (Emphasis added).

Since the invention claimed in the present application is entitled to a March 29, 1999 priority date, which is earlier than the May 10, 1999 effective filing date to which the Sodemann patent is entitled, withdrawal of the rejection under 35 U.S.C. §102(e) is respectfully requested.

Claims 1-15 were rejected under 35 U.S.C. §103(a) as being unpatentable over Lehner (W0 98/28027) in view Reinmuller (U.S. 5,077,281). This rejection is respectfully traversed.

In order for references to render a claim obvious, the references must at least suggest the features of the claim and their combination to a person having ordinary skill in the art. In the present case, the combination of references does not teach or suggest the use of taurolidine or taurultam or a mixture thereof in combination with another anti-coagulant agent to prevent thrombosis formation on a liquid-containing surface of a liquid delivery system by forming a seal in the liquid delivery system. Furthermore, the combination of references does not teach or suggest preventing thrombosis between delivery of liquids by separately contacting taurolidine or taurultam or a mixture thereof in sequential steps, alternating with another anticoagulant, and repeating the two step process between delivery of liquids via the delivery system.

Lehner discloses flushing or sealing a liquid delivery system with taurolidine or taurultam for the purpose of combating infection or sepsis. Reinmuller discloses a method for the prevention of thrombosis, teaching the use of taurolidine or taurultam as an anticoagulant contacted with a surface and further suggesting that these compounds may be used together with known anti-coagulants such as heparin. Reinmuller discloses that a single contact with taurolin is continuously effective to prevent coagulation on a surface after implantation. See Col. 4 lines 41-47.

Lehner does not teach or suggest preventing thrombosis formation. Reinmuller does not teach or suggest a method which would encompass flushing or sealing a liquid in or on the surface of a liquid delivery system. Reinmuller also does not teach or suggest a two step

process wherein the liquid containing surface of the delivery system is contacted first with an anticoagulant and second with a taurolidine or taurultam solution, wherein the two step process is repeated between periods of delivery of a liquid to a patient. In contrast to these two references, the present claims are to a method whereby thrombosis is prevented by (1) sealing a delivery system with a solution containing taurolidine or taurultam combined with an additional coagulant to prevent thrombosis formation or (2) first contacting the surface of the system with a solution containing a thrombosis-preventing amount of an anticoagulant agent other than taurolidine or taurultam and then contacting the surface with a solution containing taurolidine, taurultam or a mixture thereof, wherein the contacting steps are repeated between delivery of liquids to the patient.

Applicable case law holds that in order to render a claim obvious, the prior art must teach or suggest all of the features of the claim and their combination to a person having ordinary skill in the art.

To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. In re Vaeck, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991).

Since the combination of references cited in the Office Action does not teach or suggest any modification whatsoever of the prior art to arrive at the present invention, a finding of obviousness could only arise through some motivation to combine the references. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. In re Vaeck, 947 F.2d at 493.

Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination. ACS Hosp. Sys., Inc. v. Montefiore Hosp., 732 F.2d 1572, 1577 (Fed. Cir. 1984). A suggestion, teaching or motivation to combine the prior art references is an "essential

evidentiary component of an obviousness holding." C.R. Bard, Inc. v. MP3 Sys., Inc., 157 F.3d 1340, 1352 (Fed. Cir. 1998). Furthermore, the suggestion must be clear and particular; "broad conclusory statements about the teaching of multiple references, standing alone, are not 'evidence'". Brown & Williamson Tobacco Corp. v. Philip Morris Inc., 229 F.3d 1120, 1125 (Fed. Cir. 2000). In reversing a finding of obviousness by the Board of Patent Appeals and Interferences, the Federal Circuit recently noted that "[t]he need for specificity pervades this authority." In re Lee, 277 F.3d 1338, 1343, 61 U.S.P.Q. 2d 1430, 1433 (Fed. Cir. 2002) (emphasis added; citing In re Kotzab, 217 F.3d 1365, 1371 (Fed. Cir. 2000): "particular findings must be made as to the reason the skilled artisan , with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed.") In particular, evidence of obviousness must provide an " impetus . . . to cause one skilled in the art to combine the teachings of the references to make the proposed modification." Ex parte Levengood, 28 U.S.P.Q.2d 1300, 1301, n.2 (citing In re Albrecht, 185 U.S.P.Q. 585 (C.C.P.A. 1975)). The combination of cited art must provide evidence of the motivating force which would motivate one to do what the applicant has done.

The issue is not whether the combination could have been done, but whether the contents of the prior art references provide motivation to make the combination. Accordingly, in the present case, the PTO cannot establish obviousness by locating references which describe various aspects of Appellants' invention without also providing evidence that one skilled in the art would have been motivated to combine the separate components. Based on the pervasive authority in this area, it is well-established that the U.S. Patent and Trademark Office cannot merely assert the possibility of the combination.

In the present case, there is no motivation in the prior art for the proposed combination. First, Lehner does not serve the same purpose or function as the present invention. Lehner is concerned with the prevention of infection or sepsis, while Reinmuller and the present invention are directed to the prevention of thrombosis. There would be no motivation or suggestion for one seeking to prevent sepsis to look to the anti-thrombolytic teachings of Reinmuller. There would similarly be no motivation or suggestion for one seeking to prevent thrombosis to look to the anti-microbial teachings of Lehner.

Assuming, arguendo, that the skilled artisan examined Reinmuller in an effort to improve the teachings of Lehner, regardless of the inherent anti-coagulant activities of taurolidine or taurultam, there is nothing in Reinmuller to suggest adding an additional

anticoagulant to prevent sepsis. In analogous manner, if the skilled artisan examined Lehner in an effort to improve Reinmuller, nothing in Lehner would suggest application of an antimicrobial seal in order to prevent thrombosis. Furthermore, nothing in Lehner would suggest repeating a two step application process between delivery of liquids with a liquid delivery system.

No combination of the prior art would result in the present invention as specified in amended claim 1, since none of the prior art suggest sealing a delivery system with a solution containing taurolidine or taurultam combined with an additional coagulant, whether to prevent sepsis or thrombosis.

New claim 24 discloses a method of preventing thrombosis in a liquid-delivery system by first contacting the surface with a solution containing a thrombosis-preventing amount of an anticoagulant agent other than taurolidine or taurultam, then contacting the surface with a solution containing taurolidine, taurultam or a mixture thereof and repeating the contacting steps between delivery of liquids to the patient.

Neither reference suggests repeating such a two-step process between administration of liquids to the patient to prevent thrombosis. In fact, Reinmuller teaches that a single contact with taurolin is continuously effective to prevent coagulation on a surface after implantation. See Col. 4 lines 41-47. Thus, Reinmuller actually teaches away from the repetitive two-step process as set out in claim 24. After being led away from the present invention by the teachings of Reinmuller, nothing in Lehner would return a person having ordinary skill in the art to the concept of contacting the surface with two distinct anticoagulant compositions in sequence, repeating the process between delivery of a liquid.

There is no evidence, either in the references or the general knowledge of the prior art, of a suggestion or motivation to combine the references as set forth in the claims.

As the Federal Circuit has noted in In re Rouffet, 47 U.S.P.Q. 2d 1453 (Fed. Cir. 1998) "...an examiner may often find every element of a claimed invention in the prior art. If identification of each claimed element in the prior art were sufficient to negate patentability, very few patents would ever issue. Furthermore, rejecting patents solely by finding prior art corollaries for the claimed elements would permit an Examiner to use the claimed invention itself as a blueprint for piecing together elements in the prior art to defeat the patentability of the claimed invention." Id. at 1457. The court in Rouffet went on to state, "[t]o prevent the use of hindsight based on the invention to defeat patentability of the invention, this court

requires a showing of a motivation to combine the references that create the case of obviousness."Id. at 1457-58.

In view of the above remarks, withdrawal of the rejection based on Lehner in view of Reinmuller is respectfully requested.

Claims 1-15 were rejected under 35 U.S.C. §103(a) as being unpatentable over Lehner (W0 98/28027) in view Raad et al. (U.S. 5,688,516). This rejection is respectfully traversed.

The above-noted deficiencies of the Lehner reference are equally applicable here, and incorporated herein by reference.

The Raad et al patent discloses flushing of a catheter with heparin, and teaches other know anticoagulants. However, the Raad et al. reference cannot be combined with the Lehner reference to suggest the specifically claimed features of:

- first contacting a surface with an anticoagulant solution other than taurolidine or taurultam,
- thereafter contacting the surface with a solution containing taurolidine, taurultam or a mixture thereof, and
- repeating both of the contacting steps between delivery of liquids to the patient.

As noted above, in order for references to render a claim obvious, the references must at least suggest each of the features of the claims and their combination.

In the present case, the combination of Lehner and Raad et al. does not suggest the above-noted features or their combination. In view thereof, withdrawal of the rejection based on Lehner in view of Raad et al. is respectfully requested.

Claims 1-15 were rejected under 35 U.S.C. §103(a) as being unpatentable over Lehner and Reinmuller, in further view of Ito et al. This rejection is respectfully traversed.

The above-noted deficiencies of the Lehner and Reinmuller references are equally applicable here, and incorporated herein by reference.

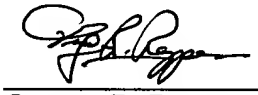
Ito is cited for disclosing the use of hirudin or a hirudin derivative that can be utilized to inhibit thrombosis on implantable and extracorporeal devices.

However, the Ito reference fails to supply any of the above-noted deficiencies of the Lehner and Reinmuller combination. In view thereof, withdrawal of the rejection based on Lehner, Reinmuller and Ito et al. is respectfully requested.

Claims 1-13 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 14-24 of U.S. Patent No. 6,258,797, in view Raad et al. In response thereto, Applicant is submitting a terminal disclaimer obviating this rejection. In view thereof, withdrawal of the rejection based on obviousness-type double patenting is respectfully requested.

Applicants submit that the present application is now in condition for allowance. Reconsideration and favorable action are earnestly requested.

Respectfully submitted,

By: 

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Marked-up Copy of Amended Claims:

1. (Twice Amended) A method of preventing thrombosis formation on a liquid-containing surface of a liquid delivery system, the liquid delivery system being connected to a patient for delivery of a liquid to said patient, the method comprising [a regimen selected from the group consisting of:

A)] forming a seal in the liquid delivery system between delivery of liquids using a thrombosis-preventing liquid containing taurolidine, taurultam or a mixture thereof, said thrombosis-preventing liquid further containing an anticoagulant agent other than taurolidine or taurultam[, and

B) first contacting surface with a solution containing a thrombosis-preventing amount of an anticoagulant agent other than taurolidine or taurultam, and thereafter contacting said surface with a solution containing taurolidine, taurultam or a mixture thereof, said surface contacting steps being repeated between delivery of liquids to said patient].

2. (Amended) The method of claim 1 wherein the [solution or] liquid containing taurolidine, taurultam or mixture thereof is contacted with said surface for at least about 1 hour.

3. (Amended) The method of claim 2 wherein said [solution or] liquid containing taurolidine, taurultam or mixture thereof is sealed in said delivery system for a period of at least 12 hours.

4. (Amended) The method of claim 3 wherein said [solution or] liquid containing taurolidine, taurultam or mixture thereof which is sealed in said delivery system, is replaced at least about daily.

13. (Amended) The method of claim 1 wherein said [solution or] liquid containing taurolidine, taurultam or a mixture thereof contains from about 0.5 to about 3% by weight of taurolidine, or from about 1 to about 7.5% by weight of taurultam.

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